

JOURNAL

THE UNITED STATES ARMY MEDICAL DEPARTMENT

PREVENTIVE MEDICINE: THE SCIENCE AND PRACTICE OF HEALTH PROTECTION

April - June 2008

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Report Documentation Page				Form Approved OMB No. 0704-0188	
Public reporting burden for the collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to a penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number.					
1. REPORT DATE JUN 2008		2. REPORT TYPE		3. DATES COVERED 00-04-2008 to 00-06-2008	
4. TITLE AND SUBTITLE The United States Army Medical Department Journal. Preventive Medicine: The Science and Practice of Health Protection				5a. CONTRACT NUMBER	
				5b. GRANT NUMBER	
				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S)				5d. PROJECT NUMBER	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Armed Forces Pest Management Board,BLDG 172, Forney Road,Silver Spring ,MD,20910-1230				8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)				10. SPONSOR/MONITOR'S ACRONYM(S)	
				11. SPONSOR/MONITOR'S REPORT NUMBER(S)	
12. DISTRIBUTION/AVAILABILITY STATEMENT Approved for public release; distribution unlimited					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT					
15. SUBJECT TERMS					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT Same as Report (SAR)	18. NUMBER OF PAGES 13	19a. NAME OF RESPONSIBLE PERSON
a. REPORT unclassified	b. ABSTRACT unclassified	c. THIS PAGE unclassified			

The Deployed Warfighter Protection Research Program: Finding New Methods to Vanquish Old Foes

CAPT Stanton E. Cope, MSC, USN
COL (Ret) Daniel A. Strickman, MS, USA
Graham B. White, PhD

INTRODUCTION

The Deployed Warfighter Protection research program (DWFP) is an initiative to develop and validate novel methods to protect United States military deployed abroad from threats posed by disease-carrying insects.¹ Vector-borne diseases such as malaria, dengue, leishmaniasis, and chikungunya are among the most important health risks facing deployed troops. There are no vaccines for many diseases transmitted by biting insects, so methods in insect management and control, as well as personal protection, are the primary tools available to protect troops.²⁻⁵

During and following World War II, scientists from the US Department of Agriculture (USDA) were regularly funded by the Department of Defense (DoD) to develop new methods and materials for controlling biting insects, particularly those that transmit diseases to humans. This highly successful collaboration produced tools that are still part of our insect-control arsenal today. Examples include:

- Deet (N,N-diethyl-3-methyl-benzamide), the primary ingredient in the majority of insect repellents available today.
- Ultra low volume application of insecticides, a methodology that distributes a limited amount of chemical per acre by optimizing the dispersion and concentration of size-limited droplets, now the standard method used by spray trucks deployed to protect neighborhoods against mosquitoes.
- Permethrin-impregnated fabrics for personal protection against the bites of ticks, mosquitoes, and other blood-feeding flying insects. Permethrin is a synthetic pyrethroid insect repellent that is used to treat uniforms, bed nets, tentage, and other fabrics.

On a global basis, many diseases transmitted by insects are increasing and spreading (eg, chikungunya, dengue, West Nile fever) or remain widespread and prevalent (eg, malaria, leishmaniasis, trypanosomiasis) despite variable vector control efforts. This situation is demonstrated in Table 1. Also, increasing numbers of species of medically important insects are developing resistance to insecticides commonly used today. For strategic reasons, therefore, there is a critical need in the DoD for the types of products USDA is uniquely able to provide. The DWFP is designed to not only encourage the rapid development of such products, but also to improve the capability of USDA to provide long-term, innovative support to military preventive medicine. In short, it is the intent of the DoD, through the DWFP, to provide funding to the USDA Agricultural Research Service (ARS) to reinvigorate this mutually beneficial working relationship between DoD and USDA, particularly as it pertains to DWFP, as defined in 2 written agreements.^{7,8}

ADMINISTRATION AND AREAS OF EMPHASIS OF THE PROGRAM

The DWFP is administered by the Research Liaison Officer of the Armed Forces Pest Management Board. The program, which was started in Fiscal Year 04, is funded at \$5 million per year. It consists of a noncompetitive funding process for USDA ARS-based research, and a competitive grants process open to non-USDA ARS scientists. Up to \$3 million per year is given to USDA ARS, specifically to National Program 104, dealing with Veterinary, Urban, and Medical Entomology. The funds are then distributed to various laboratories within the USDA system as described below.

Up to \$1.4 million is awarded each year in new competitive grants. The amount available for new

*Detailed information on the DWFP can be found at <http://www.afpmb.org/dwfpresearch.htm>.

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Table 1. Major Global Vector-borne Diseases⁶

Vectors	Diseases	Incidence, Prevalence
Mosquitoes	Malaria	Warm regions—deaths in excess of one million per year
	Lymphatic filariasis	Warm regions—infections in excess of 200 million
	Arboviruses (chikungunya, dengue, Japanese encephalitis, Rift Valley fever, West Nile virus, yellow fever, etc)	Spreading—epidemics increasing
Flies and roaches	Dysentery	Global and repetitive
Sand flies	Leishmaniasis	Focal—approximately 6 million infections a year
Fleas	Plague	Widespread—occasional outbreaks
Blackflies	Onchocerciasis (River Blindness)	Africa and Americas: focal—less than 10 million cases
Tsetse	African trypanosomiasis (Sleeping Sickness)	Africa: focal—less than 5 million cases
Reduviid bugs	Chagas disease	Americas: 24 million cases across 15 countries
Ticks and mites	Borrelioses, ehrlichias etc	Widespread
Snails	Schistosomiasis	Warm regions—Approximately 200 million cases

starts each year depends on how many projects are carried over from previous years. Grants are awarded for up to \$250,000 per year, for up to 3 years. The call for preproposals generally goes out around September. These are then reviewed by a DWFP Technical Committee, consisting of 8 to 10 members, civilian and military, representing the Army, Navy, and Air Force. Based on preproposal reviews, investigators may be asked to submit a full proposal. In November, the DWFP Committee convenes for a 2-day review of the USDA research and to determine which new competitive grants will be awarded. Final competitive award winners are usually notified in December.

The DWFP research portfolio is concentrated in 3 specific areas: novel insecticide chemistries/formulations, application technology, and personal protective systems. The first area includes discovery of new active ingredients, tests of existing insecticides on pests and vectors of public health importance, especially mosquitoes and sand flies, and reformulation of existing insecticides to improve efficacy or delivery.

INVOLVEMENT OF THE US DEPARTMENT OF AGRICULTURE

The USDA ARS has been a partner in DWFP since 2004, but cooperation between the nation's agricultural research and the military goes back many decades. World War II was a unique moment in this relationship. American forces were faced with the usual disease challenges of warfare, but, for the first time, scientific understanding and industrial capacity combined to offer hope of preventing those diseases caused by vector-borne pathogens. The USDA Bureau of Entomology and Plant Quarantine laboratory in Orlando⁹ targeted the flea vectors of plague, the louse vectors of typhus, the chigger vectors of scrub typhus, mosquitoes including vectors of malaria and yellow fever,¹⁰ as well as bedbugs, cockroaches, flies, and ticks.¹¹ In just a few years, the laboratory refined the uses of DDT* as a control agent for public health pests and of repellent chemicals (ethyl hexanediol, dimethyl phthalate, dimethyl carbate, indalone, and benzyl benzoate) as topical and clothing repellents. Workers at the Beltsville Center invented the insecticidal

*1,1,1-trichloro-2,2-bis(p-chlorophenyl)ethane or Dichloro-diphenyl-trichloroethane

aerosol bomb¹² (precursor of all spray cans) for military use during WWII, and collaborated with the Orlando Lab to invent the repellent deet¹³ in 1947.

The USDA continued to collaborate with the military through the 1970s and 1980s, most notably working out the means for permethrin treatment of military uniforms.¹⁴⁻¹⁶ Concentration on military problems slowed, eventually reduced to the development of repellent active ingredients and improved trapping systems. The DWFP effort brought greater focus in 3 ways. First, it provided significant funds (\$3 million per year) to the USDA ARS for research. Second, it defined the subject areas of most interest to the military, namely new toxicants for public health pests, new application equipment for pesticides, and new personal protection system. Finally, the DWFP established mechanisms of communication between the military and the USDA ARS that have kept both sides engaged in the conversation on the direction of research required to produce products for the protection of military personnel from arthropods that transmit pathogens.

During the last 3 years we have conceived and executed the concept of a “virtual laboratory” that takes advantage of the core strengths of the USDA ARS at each of the laboratories to establish a smooth flow for development of new vector control products. Chemical discovery proceeds from several strategies that are, for the most part, based on basic science rather than bulk screening. Promising candidates emerge from bioassays, leading to more comprehensive evaluation against target insects. Once we have what we think is a useful chemical, we consider how best to use it against target insects in an integrated pest and disease management program. With those goals in mind, we have in the past approached individual private companies in order to form a partnership for further development. In that case, it is up to the company to formulate the active ingredient. Recently, we have been performing research on formulation, reasoning that a preparation closer to product status may be more attractive for industrial development. We are also working on regulatory issues by funding a position on public

health pesticides with IR-4*, the USDA-funded entity that supports registration of pesticides for use on specialty crops.¹⁷

Some USDA ARS laboratories and investigators have had only a temporary involvement with DWFP, depending mainly on whether the core agricultural mission of their unit effectively synergized the military mission of the funds. Currently, there are 5 laboratories that receive DWFP funding. The following sections discuss some of the work underway in those laboratories.

Invasive Insect Biocontrol and Behavior Laboratory

The Invasive Insect Biocontrol and Behavior Laboratory in Beltsville, Maryland, is the laboratory that first patented deet¹³ the dominant active ingredient in American insect repellents. It continues to be well-equipped to perform any level of synthetic and analytical chemistry, an obvious advantage for a laboratory attempting to discover new toxicants and repellents. Chauhan and colleagues¹⁸ have been involved in the discovery of promising new repellent active ingredients, mosquito larvicides, and exciting new insecticidal chemistries. He takes advantage of a small *Aedes aegypti* colony on site and performs simple, screening bioassays to guide his work. Another research team is at the cutting edge of research on how mosquitoes detect hosts.¹⁹ Using molecular biology and electrophysiology, they will develop tools that dissect biting behavior into its component, physiological parts. Combined with the synthetic chemistry of the laboratory, this work will provide very precise pathways for discovering entirely new behavior-altering chemicals. Potential products could be chemicals that selectively repel infected mosquitoes, chemicals that induce mosquitoes to bite nonhuman hosts, and powerful attractants that could be combined with toxicants.

Mosquito and Fly Research Unit

Scientists at the Mosquito and Fly Research Unit (MFRU) in Gainesville, Florida, are experts on many aspects of the biology and control of mosquitoes and flies. Their work includes the following:

*Interregional Research Project No 4 (IR-4), the Minor Crop Pest Management Program, is the principal public effort supporting the registration of crop protection products and biological pest control agents for approximately \$40 billion minor crop industry. Source: USDA Cooperative State Research, Education, and Extension Service, http://www.csrees.usda.gov/nea/pest/in_focus/ipm_if_minor.html

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- Toxicant discovery by Pridgeon et al²⁰ includes tests of registered toxicants that have not yet been applied for public health pests. They also work with industry to explore the effectiveness of new compounds that have not been used as insecticides. Promising chemicals have also been extracted from native plants.
- Pridgeon and associates²¹ have invented an entirely new class of “molecular pesticides” that promise to combine great safety, flexibility, and specificity.^{22,23}
- Bernier and colleagues have extended fundamental work to the production of inhibitors for mosquitoes (patent pending) and powerful attractants for flies²⁴ and mosquitoes.²⁵ Collaborators at the University of Florida are using computational chemistry (QSAR/QSPR*) to reanalyze pesticide bioassay data generated over 50 years at the Orlando and Gainesville laboratories, resulting in synthesis of repellents with 3-fold longer repellency than deet.²⁶
- Researchers Cooperband and Allen²⁷ have also explored the effects of sublethal dosages of pesticides on mosquito behavior using quantitative interpretation of videos, extending our knowledge of how best to apply residual insecticides.
- Research is underway on fly control, including trapping and toxicants, at field sites in the United States and middle eastern locations.
- The Center for Medical, Agricultural, and Veterinary Entomology, which includes the MFRU, has been very active in developing field tests sites, including Thailand; Kenya; Camp Blanding, Florida; and the Coachella Valley, California. The MFRU works closely with the Navy Entomology Center of Excellence at the US Naval Air Station, Jacksonville, Florida, especially for field testing and evaluation of application equipment.

Biological Control of Pests Research Unit

At the Biological Control of Pests Research Unit (BCPRU) in Stoneville, Mississippi, Lyn and Streett²⁸ collaborate with scientists at the MFRU and industry to develop formulations of public health pesticides. Also, the BCPRU has facilities for pilot production of biopesticides.

*Quantitative structure-activity relationship/quantitative structure-property relationship

Natural Products Utilization Research Unit

The Natural Products Utilization Research Unit in Oxford, Mississippi, has a history of working in partnership with the University of Mississippi School of Pharmacy on the discovery of natural sources of bioactive compounds. The unit goes beyond simple extracts to complex analysis of families of chemicals and optimization through synthesis of series of compounds. Thanks to DWFP funding, USDA was able to leverage the effort by transferring funds to the University of Mississippi for insecticide development. Cantrell and colleagues^{29,30} have already been involved in discovery and patent of repellents and toxicants. The products of their research will be screened on site using a new and very simple bioassay developed by Becnel and Pridgeon³¹ at the MFRU. Promising candidates will be evaluated in more detail by the MFRU.

Areawide Pest Management Research Unit

Hoffmann and associates^{32,33} at the Areawide Pest Management Research Unit (APMRU) in College Station, Texas, have worked closely with the MFRU and the Navy Entomology Center of Excellence to systematically evaluate the droplet spectra of a wide range of application equipment. The data have already informed the military on the best equipment for its purposes. Also, Nachman's³⁴ completed work on neuropeptides of public health pests, including mosquitoes, ticks, and flies, has established an entirely new potential mechanism for insecticidal mode of action.

COMPETITIVE AWARD HIGHLIGHTS

Publicly posted on the federal government's website[†] announcing grant availability, DWFP requests for preproposals have yielded an average of 38 submissions annually, from academics, military entomologists, industry, and others around the world. More than one-third of these have been invited to prepare full proposals, from which 34 projects, shown in Table 2, have been selected for grant funding during the first 5 years of the program. The range of topics and the quality of many proposals have been impressive. Indeed, many of the intended products could find wider applications for public health and veterinary pest control. So far, the smallest grant value was \$22,552 over 2 years, while some grants have

† <http://www.grants.gov/>

Table 2. Deployed Warfighter Protection Research Program Competitive Project Grants

Award Recipient	Purpose	Org*	Highlights
2004 (n=8)			
CDR Claborn (Dr Walker)	Sprayer diesel conversion	M	2 prototypes & NSN [†]
LTC Coleman	Sand Fly control-Iraq	M	Improved field operations
LCDR Hoffman	Mosquito control with UAV [‡]	M	Passed to USAF
Prof Phil Koehler	Filth & Biting Fly control	A	1 NSN [†] & 2 deployed citations
Dr Bob Peterson	Comparative risk analyses	A	Publications & public appreciation
Dr Steve Presley	Hollow fiber impregnated fabric	A	Novel technology
Dr Bill Reifernath	Repellent synergy	D	Cancelled
Dr Ed Rowton	Sand Fly control-laboratory	M	Essential collaborations
2005 (n=7)			
Prof Chas Apperson	Dengue vector ovitrap	A	Duty under instruction student
Prof Lane Foil	Targeted sand fly control	A	WRAIR [§] collaboration
LT Haagsma	Mosquito control with UAV [‡]	M	Passed to USDA ARS APMRU
Dr Que Lan	Novel mosquito insect growth regulator	A	Product licensed
Dr Mike Scharf	Low molecular weight insecticides	A	Industry support
LT Stancil (LCDR Florin)	Dengue vector larval control	M	EPA [¶] registration in preparation
Prof Alon Warburg	Sand Fly control military camps	A	WRAIR [§] collaboration
2006 (n=6)			
Bruce Dorendorf	Diesel backpack	D	NECE** collaboration
Bruce Dorendorf	Ultra low volume nozzle	D	NECE** collaboration
Dave Malone	New ultra low volume adulticide etofenprox	D	EPA [¶] registration in progress
Dr Phil Kaufman	Novel compounds	A	Duty under instruction student
Dr Bob Peterson	Comparative risk analyses	A	Strategic appreciation
Dr Gaby Zollner	Novel vapor repellent	M	Delayed
2007 (n=3)			
Dr Ed Rowton	Sand Fly control—WRAIR [§] laboratory	M	Essential collaborations
MAJ Richardson	Sand Fly insectary, USAMRU-K ^{††}	M	Pioneering service
Dr Dolan & Dr McAllister	Natural product pesticides	G	CDC-NCZVED ^{‡‡} collaborations
2008 (n=10)			
Bruce Dorendorf	Ultra low volume backpack diesel system	D	
Prof Lane Foil	Sand Fly larval control	A	
MAJ Stephen Frances	Australia field repellent fabrics	M	
Philipp Kirsch	Adulticides targeting Sand Flies	D	
Prof Phil Koehler	Military protections vs Filth Flies	A	
Richard Poche	Host-target insecticides vs Sand Flies	D	
LT Richardson	Novel tools & strategies vs <i>Ae.aegypti</i>	M	
Prof Masoud Salyani	Spray methods vs Sand Flies	A	
Prof Alon Warburg	Phlebotomine control	A	
Dr Mike Willis	Formulate UW4015 larvicide	D	

*Type of organization:

A – Academia (n=14) D – Industry (n=8)

M – Military (n=11) G – Other government (n=1)

[†]National Stock Number

[‡]Unmanned aerial vehicle

[§]Walter Reed Army Institute of Research

[¶]US Environmental Protection Agency

**Navy Entomology Center of Excellence

^{††}US Army Medical Research Unit, Kenya

^{‡‡}US Centers for Disease Control and Prevention–National Center for Zoonotic, Vector-Borne, and Enteric Diseases

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exceeded \$200,000 per year for 3 years. Awardees are encouraged to seek patents and find licensees for their products, several of which are already nearing commercialization.

For example, in 2005 a grant was awarded to ADAPCO (Sanford, Florida) to develop etofenprox³⁵ for use as mosquito ultra low volume (ULV) adulticide. This chemical, a nonester pyrethroid manufactured by the Mitsui Group in Japan and licensed to Central Life Sciences (Schaumburg, Illinois) for US registration for public health applications, is far less toxic to humans, animals, and birds than most other insecticides currently used for mosquito control.³⁶ It is expected to receive EPA approval for marketing this year.

Although the DWFP program prioritizes the discovery and development of agents for use against blood-feeding adult mosquitoes and biting flies that would afflict deployed military personnel, some research grants have been awarded for development of chemicals with new modes of action against mosquito developmental stages in water. At the University of Wisconsin, Madison, Lan and colleagues³⁷⁻⁴¹ had the idea to block sterol carrier proteins that are metabolically essential for the nutrition and growth of mosquito larvae. After screening tens of thousands of candidate compounds, they discovered several with the power to block mosquito sterols, effectively serving as growth inhibitors. The most appropriate compound has been licensed by a commercial company where it is being formulated for applied use. Both phases of the work have been supported by DWFP grants.

Among DWFP grants awarded to scientifically qualified military officers, the first was for adapting an unmanned aerial vehicle, shown in Figure 1, to carry application equipment for delivery of larvicidal granules or ULV adulticide. This project originated with the Disease Vector Ecology and Control Center (now the Navy Entomology Center of Excellence) at the Jacksonville Naval Air Station, where capabilities were demonstrated, then adopted by the USAF Aerial Spray Unit* at Youngstown, Ohio. To further develop this application technology with an unmanned aerial vehicle platform made in the United States, the project has been transferred to the Application Technology Laboratory of the USDA ARS at the APMRU. This relay of progressive research and development steps

*See related article on page 54.



Figure 1. Yamaha RMax unmanned aerial vehicle fitted with ULV spray nozzles (top) and with twin hopper (bottom) for application of granular larvicide to control mosquitoes.

has been facilitated by DWFP funds and objectives to meet one of the strategic DoD goals of fielding unmanned vehicles.

Also by collaboration with the Navy Entomology Center of Excellence, a series of DWFP grants have enabled Dorendorf Advanced Technologies, Inc (Winnebago, Minnesota) to design and build new sprayers using military fuels instead of gasoline. The first backpack system, shown in Figure 2, operates almost silently with compressed air from cylinders charged by a diesel-fuelled compressor which also drives a truck-mounted ULV sprayer, the Terminator™. In addition to the strategic advantages of silent spraying, a unique ULV nozzle is being created for the backpack system. Altogether, this

purpose-built, diesel-fuelled spray equipment will allow troops to be deployed with battlefield-ready spray equipment for vector control.

From diverse proposals for better insect repellency of fabrics to protect military personnel, one DWFP grant was awarded to researchers at the Institute of Environmental and Human Health, Texas Tech University, Lubbock, Texas. That ingenious project developed a new type of permethrin-impregnated hollow fiber capable of being integrated with many textiles. This durable microcapillary can serve as a convenient carrier fiber for weaving the repellent and insecticidal powers of permethrin into any fabrics used for making clothes, curtains, tents, and other protective layers.*

Two DWFP projects have employed pyriproxyfen, the most powerful insect growth regulator (IGR), against dengue vector mosquitoes. In the Peruvian Amazon community at Iquitos, Stancil⁴² (Naval Medical Research Center Detachment, Peru) received a grant to optimize strategies for preventing the breeding of *Aedes aegypti* mosquitoes in containers of water. The project ran for 3 years, and involved collaboration with Peruvian scientists and researchers from the University of California and Rothamsted Research, United Kingdom. In addition to simply stopping the breeding of mosquitoes in treated habitats, effective quantities of pyriproxyfen IGR are transferred from one container to another by mosquito females as they go from site to site laying their eggs, thus impacting more habitats than were treated directly. Mosquito population suppression across whole suburbs of the city has effectively prevented dengue transmission without the need to spray adulticides. Building on that achievement, researchers at the Armed Forces Research Institute of Medical Sciences, Bangkok,⁴³ in



Figure 2. The first backpack ULV sprayer system developed under DWFP grants operates almost silently with compressed air from cylinders.

conjunction with local military personnel in Thailand, are now evaluating several devices treated with pyriproxyfen IGR for protecting military camps against *Aedes aegypti* and the arboviruses transmitted by this widespread domestic mosquito (see Table 1).

The biggest emphasis of DWFP projects has been to find ways to combat *Phlebotomus* sand flies (Figure 3) which are problematic in many parts of the Middle East. These small hairy flies transmit *Leishmania* parasites that cause disfiguring sores (Figure 4) which fester for many months and require long-term medication. Some forms

of the infection go to the liver and can be fatal. More than a thousand US personnel have contracted leishmaniasis during ongoing Operations Enduring Freedom and Iraqi Freedom.⁴⁴ Unfortunately, the types of insecticide sprays that normally control mosquitoes are generally ineffective against sand flies. To address this threat, DWFP grants were channeled, by competitive award, via the Entomology Division at the Walter Reed Army Institute of Research to facilitate

intensive field studies of sand fly behavior and control. Although a series of research papers by Coleman, Burkett, and colleagues⁴⁵⁻⁴⁷ have resulted, the sand fly biting problem has not been resolved. Consequently, efforts to understand how to improve the delivery of more effective insecticidal sprays are being reemphasized. Also, Warburg and colleagues⁴⁸ at the Kuvim Center of the Hadassah Medical School, Jerusalem, received a DWFP grant to



Figure 3. *Phlebotomus* sand fly (Photo courtesy of Ed Rowton, PhD)

develop measures to protect outposts against sand flies. These projects have revealed that sand flies often emerge from the soil beneath tents and camps. In an effort to prevent sand flies breeding in rodent burrows, the Genesis Company (Wellington, Colorado) won an award for producing insecticidal baits that would pass through specific rodent reservoir hosts of leishmaniasis to prevent breeding of sand fly larvae in their burrows. This approach is being developed with other feed-through treatments by Mascari et al⁴⁹⁻⁵¹ at Louisiana

*Project results unpublished to date

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Figure 4. Examples of dermal leishmaniasis contracted in Iraq during Operation Iraqi Freedom. Note in the top photo that the area of the arm covered by the shirt sleeve is free of bites, demonstrating the value of simple measures in the prevention of insect bites. (Photos courtesy of COL Russell Coleman, MS, USA)

State University for field testing against sand flies in Turkey.

Control of filth flies and house flies is best achieved by good sanitation, but this cannot always be ensured in deployment situations. One competitive DWFP award enabled Koehler⁵² and military students in the Urban Entomology Unit of the Department of Entomology and Nematology at the University of Florida, Gainesville, to optimize some old countermeasures for fly control. For example, one student evaluated pesticides for residual treatments of various types of string and rope on which flies like to rest. He determined which combination of insecticide and string fiber would be most effective for use against flies in tented camps. Another student continues this line of experimentation by devising ways to drape loops of treated string over attractant traps to which flies are lured and killed. These masters level graduate students were supported by the US Navy's Medical

Service Corps Inservice Procurement Program.⁵³ Another development from Koehler's team, invisible imidacloprid paint bait with attractant for killing flies quickly, was the first DWFP product to receive a National Stock Number from the Armed Forces Pest Management Board.

As the DWFP competitive grants program has grown, awardees have included entomologists at the US Centers for Disease Control, Division of Vector-Borne and Zoonotic Diseases, for development of natural pesticides extracted from agricultural waste. Other plant products that have insect repellent properties are under evaluation for insecticidal potency against flies, mosquitoes, and sand flies, while Scharf and Song^{54,55} are exploring low molecular weight compounds that could serve as volatile repellents and insecticides for potential limitation of biting insects over a wide area.

Although the public perception of pesticides can be unfavorable, the facts are that the use of pesticides can be extremely effective against all sorts of pests and disease vectors. In an effort to investigate this dichotomy, one of the most original lines of inquiry funded by DWFP competitive grants has allowed Peterson and colleagues⁵⁶⁻⁶¹ at Montana State University, Bozeman, to undertake comparative risk analyses of the impact of pesticides. For a series of model scenarios involving vector-borne diseases such as malaria, West Nile fever, and plague, they carefully quantified the likely benefits of vector control by means of appropriate insecticide applications, versus possible disadvantages to the health of people and environmental impact. One particular study by Macedo et al⁶² weighed the potential health benefits of vector control against the adverse consequences of likely exposure of deployed military personnel to pesticides used on clothing and bed nets, and sprayed around the camp. In all cases, the risk to humans was found to be minimal compared with the health benefits of avoiding vector-borne diseases.

UPGRADING DEFENSE AGAINST DISEASES TRANSMITTED BY INSECT BITES

While many useful products from DWFP research are already on the way towards production and supply for the public as well as deployed troops, the examples described above are far from sufficient to cover all our needs. Apart from combating mosquitoes and the various types of flies that transmit debilitating

infections such as malaria, leishmaniasis, dengue, and other arboviruses, there are many other noxious types of biting insects (bedbugs, fleas, lice, etc) and other arthropods (ticks, mites, scorpions, etc) that merit our concern. With nearly 5 years of progress in the DWFP program, however, our focus remains on the most dangerous flying vectors, particularly certain species of mosquitoes and sand flies. That focus is necessary until we have greatly improved methods and materials to protect our forces deployed to forward situations in all regions of the world from the threats of inconspicuous insect foes. This will allow those forces to more effectively deal with the challenges presented by the more obvious human enemies.

REFERENCES

1. Agriculture Research Service research page. US Dept of Agriculture website. Deployed war-fighter protection (DWFP) program. January 2007. Available at: <http://www.ars.usda.gov/Research/docs.htm?docid=14013>. Accessed May 1, 2008.
2. Coates JB, ed-in-chief. Communicable diseases, malaria. Washington, DC: Office of The Surgeon General, US Dept of the Army; 1963. Hoff EC, ed. *Preventive Medicine in World War II*; vol 6.
3. Dickens T. Vector control as a force multiplier. *Defense* 90. September/October 1990:26-35.
4. *Technical Guide 36, Personal Protective Techniques Against Insects and Other Arthropods of Military Importance*. Washington, DC: US Armed Forces Pest Management Board. 2003. Available at: http://www.afpmb.org/coweb/guidance_targets/ppms/TG36/TG36.htm.
5. Debboun M, Robert L, O'Brien L, Johnson R, Berté S. Vector control and pest management. *Army Med Dept J*. 2006;24:31-39.
6. Service MW, ed. *The Encyclopedia of Arthropod-transmitted Infections*. Wallingford, Oxfordshire, United Kingdom: CABI; 2001.
7. Master Memorandum of Understanding Between United States Department of Defense and United States Department of Agriculture Relative to Cooperation with Respect to Food, Agriculture, Pest Management, Nutrition, Related Homeland Security Requirements, and other Research of Mutual Interest. Washington, DC: US Dept of Agriculture & US Dept of Defense; March 14, 2003. Available at: http://www.afpmb.org/pubs/misc/mastr_usda.pdf.
8. Supplement to Master Memorandum of Understanding Between US Department of Defense and US Department of Agriculture, Relative to Cooperation with Respect to Food, Agriculture, Pest Management, Nutrition, Related Homeland Security Requirements, and other Research of Mutual Interest. Washington, DC: US Dept of Agriculture & US Dept of Defense; February 5, 2004. Available at: <http://www.afpmb.org/pubs/misc/MMOU-Supplement.pdf>.
9. Knipling EF. Insect control investigations of the Orlando, Fla, laboratory during World War II. *Smithson Rep for 1948*. Washington, DC: Smithsonian Institution; 1949:331-348. Smithsonian Publication 3968.
10. King WV. *Chemicals evaluated as insecticides and repellents at Orlando, FLA; Agricultural Handbook No. 69*. Washington, DC: Agricultural Research Service, US Dept of Agriculture; 1954.
11. *Materials Evaluated as Insecticides, Repellents, and Chemosterilants at Orlando and Gainesville, FLA, 1952-1964. Agricultural Handbook No. 340*. Washington, DC: Agricultural Research Service, US Dept of Agriculture; 1967.
12. Sullivan WN. The coupling of science and technology in the early development of the World War II aerosol bomb. *Mil Med*. 1971;136(2):157-158.
13. McCabe ET, Barthel WF, Gertler SI, Hall SA. Insect repellents, III. N, N-diethylamides. *J Org Chem*. 1954;19:493-498.
14. Schreck CE, Posey K, Smith D. Durability of permethrin as a potential clothing treatment to protect against blood-feeding arthropods. *J Econ Entomol*. 1978;71:397-400.
15. Schreck CE, Smith N, McGovern TP. Repellency of selected compounds against two species of biting midges (Diptera: Ceratopogonidae: *Culicoides*). *J Med Entomol*. 1979;16:524-527.
16. Schreck CE, Snoddy EL, Spielman A. Pressurized sprays of permethrin or DEET on military clothing for personal protection against *Ixodes dammini* (Acari: Ixodidae). *J Med Entomol*. 1986;23:396-399.
17. IR-4 Project website. Available at: <http://www.ir4.rutgers.edu/index.html>.
18. Chauhan KR, Klun JA, Debboun M, Kramer M. Feeding deterrent effects of catnip oil components compared with two synthetic amides against *Aedes aegypti*. *J Med Entomol*. 2005;42(4):643-646.

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19. Nichols Z, Vogt RG. The SNMP/CD36 gene family in Diptera, Hymenoptera and Coleoptera: *Drosophila melanogaster*, *D. pseudoobscura*, *Anopheles gambiae*, *Aedes aegypti*, *Apis mellifera*, and *Tribolium castaneum*. *Insect Biochem Mol Biol*. 2008;38:398-415.
20. Pridgeon JW, Pereira RM, Becnel JJ, Allan SA, Clark GG, Linthicum KJ. Susceptibility of *Aedes aegypti*, *Culex quinquefasciatus* Say, and *Anopheles quadrimaculatus* Say to 19 pesticides with different modes of action. *J Med Entomol*. 2008;45(1):82-87.
21. Pridgeon JW, Becnel JJ, Strickman DA, inventors. New method for developing molecular pesticides. Patent application serial number 11/716,499 Docket #0122.06, March 9, 2007. Information available at: <http://www.ars.usda.gov/research/patents/patents.htm?serialnum=11716499>.
22. Zhao L, Pridgeon JW, Becnel JJ, Clark GG, Linthicum KJ. Cytochrome c gene and protein expression: developmental regulation, environmental response, and pesticide sensitivity in *Aedes aegypti*. *J Med Entomol*. 2008;45:401-408.
23. Pridgeon JW, Zhao L, Becnel JJ, Strickman DA, Clark GG, Linthicum KJ. Topically applied *AaeIAP1* double-stranded RNA kills female adults of *Aedes aegypti*. *J Med Entomol*. 2008;45:414-420.
24. Quinn BP, Bernier UR, Geden CJ, Hogsette JA, Carlson DA. Analysis of extracted and volatile components in blackstrap molasses feed as candidate housefly attractants. *J Chromatograph A*. 2007;1139(2):279-284.
25. Katritzky AR, Wang Z, Slavov S, Tsikolia M, Dobchev D, Akhmedov NG, Hall CD, Bernier UR, Clark GG, Linthicum KJ. Synthesis and bioassay of improved mosquito repellents predicted from chemical structure. *Proc Natl Acad Sci USA*. 2008;105(21):7359-7364.
26. Bernier UR, Allan SA, Quinn BP, Kline DL, Barnard DR, Clark GG. Volatile compounds from the integument of White Leghorn Chickens (*Gallus gallus domesticus* L.): candidate attractants of ornithophilic mosquito species. *J Sep Sci*. 2008;31:1092-1099.
27. Cooperband MF, Allan SA. Behavioral definitions, "excito-repellency," and is meaning with respect to mosquito contact with treated surfaces. *Abstract 242 of the 74th Annual Meeting, American Mosquito Control Association, Sparks, Nevada. 2-6 March 2008*. Mount Laurel, NJ: American Mosquito Control Association; 2008:44. Available (registration required) at: <http://www.afpmb.org/pubs/dwfp/meetings/amca2008/224-cooperband.pdf>.
28. Lyn ME, Streett D, Becnel J. New mosquito biolarvicide formulation for improved residual activity. *Abstract 242 of the 74th Annual Meeting, American Mosquito Control Association, Sparks, Nevada. 2-6 March 2008*. Mount Laurel, NJ: American Mosquito Control Association; 2008:47.
29. Cantrell CL, Klun JA, Bryson CT, Kobaisy M, Duke SO. Isolation and identification of mosquito bite deterrent terpenoids from leaves of American (*Callicarpa americana*) and Japanese (*Callicarpa japonica*) beautyberry. *J Agric Food Chem*. 2005;53:5948-5953.
30. Pridgeon JW, Meepagala KM, Becnel JJ, Clark GG, Pereira RM, Linthicum KJ. Structure-activity relationships of 33 piperidines as toxicants against female adults of *Aedes aegypti* (Diptera: Culicidae). *J Med Entomol*. 2007;44(2):263-269.
31. Becnel JJ, Pridgeon JW. A high throughput screening method to identify potential pesticides for mosquito control. *J Med Entomol*. In press.
32. Hoffmann WC, Walker TW, Smith VL, Martin DE, Fritz BK. Droplet-size characterization of handheld atomization equipment typically used in vector control. *J Am Mosq Control Assoc*. 2007;23:315-320.
33. Hoffmann WC, Walker TW, Martin DE, Barber JA, Gwinn T, Smith VL, Szumlas D, Lan Y, Fritz BK. Characterization of truck-mounted atomization equipment typically used in vector control. *J Am Mosq Control Assoc*. 2007;23:321-329.
34. Nachman RJ. Invertebrate Neuropeptides VIII. Introduction. *Peptides*. 2008;29:149-151.
35. World Health Organization. *Report of the 3rd WHOPES Working Group Meeting, 23-24 September 1999; Review of: Deltamethrin 1%SC and 25%WT; Etofenprox 10%EC and 10%EW*. Geneva, Switzerland: World Health Organization; 1999: Document CDS/CPE/WHOPES/99.4.
36. Croft AM, Baker D, von Bertele MJ. An evidence-based vector control strategy for military deployments: the British Army experience. *Med Trop (Mars)*. 2001;61:91-98.
37. Lan Q, Wessely V. Expression of a sterol carrier protein-x gene in the yellow fever mosquito, *Aedes aegypti*. *Insect Mol Biol*. 2004;13:519-529.
38. Blitzer EJ, Yazunova I, Lan Q. Functional analysis of AeSCP-2 using gene expression knockdown in the yellow fever mosquito, *Aedes aegypti*. *Insect Mol Biol*. 2005;14:301-307.

39. Kim MS, Wessely V, Lan Q. Identification of mosquito sterol carrier protein-2 inhibitors. *J Lipid Res.* 2005;46:650-657.
40. Vyazunova I, Wessley V, Kim M, Lan Q. Identification of two sterol carrier protein-2 like genes in the yellow fever mosquito, *Aedes aegypti*. *Insect Mol Biol.* 2007;16:305-314.
41. Larson RT, Wessely V, Jiang Z, Lan Q. Larvicidal activity of sterol carrier protein-2 inhibitor in four species of mosquitoes. *J Med Entomol.* 2008;45(3):439-444.
42. Sihuincha M, Zamora-Perea E, Orellana-Rios W, Stancil JD, Lopez-Sifuentes V, Vidal-Oré C, Devine GJ. Potential use of pyriproxyfen for control of *Aedes aegypti* (Diptera: Culicidae) in Iquitos, Peru. *J Med Entomol.* 2005;42(4):620-630.
43. Armed Forces Research Institute of Medical Sciences website. Available at: <http://www.afirms.org>. Accessed May 1, 2008.
44. Aronson NE. Leishmaniasis in relation to service in Iraq/Afghanistan, U. S. armed forces, 2001-2006. *Med Surveill Mon Rep.* 2007;14(1):2-5.
45. Coleman RE, Burkett DA, Putnam JL, et al. Impact of phlebotomine sand flies on US military operations at Tallil Air Base, Iraq: 1. background, military situation, and development of a leishmaniasis control program. *J Med Entomol.* 2006;43(4):647-662.
46. Coleman RE, Burkett DA, Sherwood V, et al. Impact of phlebotomine sand flies on US military operations at Tallil Air Base, Iraq: 2. temporal and geographic distribution of sand flies. *J Med Entomol.* 2007;44(1):29-41.
47. Burkett DA, Knight R, Dennett JA, Sherwood V, Rowton E, Coleman RE. Impact of phlebotomine sand flies on US military operations at Tallil Air Base, Iraq: 3. evaluation of surveillance devices for the collection of adult sand flies. *J Med Entomol.* 2007;44(2):381-384.
48. Jaffe CL, Baneth G, Abdeen ZA, Schlein Y, Warburg A. Leishmaniasis in Israel and the Palestinian Authority. *Trends Parasitol.* 2004;20:328-332.
49. Mascari TM, Mitchell MA, Rowton ED, Foil LD. Evaluation of novaluron as a feed-through insecticide for control of immature sand flies (Diptera: Psychodidae). *J Med Entomol.* 2007;44(4):714-717.
50. Mascari TM, Mitchell MA, Rowton ED, Foil LD. Laboratory evaluation of diflubenzuron as a feed-through for control of immature sand flies (Diptera: Psychodidae). *J Med Entomol.* 2007;44(2):171-174.
51. Mascari TM, Mitchell MA, Rowton ED, Foil LD. Ivermectin as a rodent feed-through insecticide for control of immature sand flies (Diptera: Psychodidae). *J Am Mosq Control Assoc.* 2008;24(2):323-326.
52. Koehler P. DWFP fly control research. Paper presented at: 2007 DoD Pest Management Workshop; February 12-16, 2007; Jacksonville Naval Air Station, Florida. Available at: <http://www.afpmb.org/meetings/TriService2007/Presentations/Wednesday/BOQAfternoon/Koehler.ppt>.
53. *OPNAV Instruction 1420.1A; Enlisted to Officer Commissioning Programs Application Administrative Manual*. Washington, DC: Office of the Chief of Naval Operations, US Dept of the Navy; May 2, 2003: chap 6.
54. Scharf ME, Nguyen SN, Song C. Evaluation of volatile low molecular weight insecticides using *Drosophila melanogaster* as a model. *Pest Manag Sci.* 2006;62:655-663.
55. Nguyen SN, Song C, Scharf ME. Toxicity, synergism, and neurological effects of novel volatile insecticides in insecticide-susceptible and -resistant *Drosophila* strains. *J Econ Entomol.* 2007;100:534-544.
56. Peterson RK, Macedo PA, Davis RS. A human-health risk assessment for West Nile virus and insecticides used in mosquito management. *Environ Health Perspect.* 2006;114(3):366-372.
57. Davis RS, Peterson RK, Macedo PA. An ecological risk assessment for insecticides used in adult mosquito management. *Integr Environ Assess Manag.* 2007;3:373-382.
58. Antwi F, Shama LM, Peterson RKD. Risk assessments for the insect repellents DEET and picaridin. *Regul Toxicol Pharmacol.* 2008;51(1):31-36.
59. Schleier JJ, Shama LM, Davis RS, Macedo PA, Peterson RKD. Equine risk assessment for insecticides used in adult mosquito management. *Hum Ecol Risk Assess.* 2008;14:392-407.
60. Schleier JJ, Peterson RKD, Macedo PA, Brown DA. Environmental concentrations, fate, and risk assessment of pyrethrins and piperonyl butoxide after aerial ultra-low-volume applications for adult mosquito management. *Environ Toxicol Chem.* 2008;27:1063-1068.

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61. Schleier JJ, Macedo PA, Davis RS, Shama LM, Peterson RKD. A two-dimensional probabilistic acute human-health risk assessment of insecticide exposure after adult mosquito management. *Stoch Environ Res Risk Assess.* 2008; 22, doi:10.1007/s00477-008-0227-5.
62. Macedo PA, Peterson RK, Davis RS. Risk assessments for exposure of deployed military personnel to insecticides and personal protective measures used for disease-vector management. *J Toxicol Environ Health.* 2007;70(20):1758-1771.

AUTHORS

CAPT Cope is the Research Liaison Officer of the Armed Forces Pest Management Board, Washington, DC.

COL (Ret) Strickman is the National Program Leader, Program 104: Veterinary, Medical, and Urban Entomology at the US Dept of Agriculture, Agricultural Research Service, Beltsville, Maryland.

Dr White is Technical Consultant for the Deployed Warfighter Protection Research Program, based at the Mosquito and Fly Research Unit, Center for Medical, Agricultural, and Veterinary Entomology, USDA Agricultural Research Service, Gainesville, Florida.



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COL Dunemn joins the board replacing COL Patricia Patrician, AN, USA. COL Patrician has been a member of the Board since October, 2004. We thank COL Patrician for her dedication to the high standards and professional quality of this publication, and her years of service and support to our mission.

The Editors

